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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/316,001	05/21/1999	ROGER V. KENDALL	FSC-6	7220

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	33

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/316,001	Kendall et al.
Examiner	**Art Unit**
G.R. Ewoldt, Ph.D.	1644

-- ***The MAILING DATE of this communication appears on the cover sheet with the correspondence address*** --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *2/24/03 and 4/04/03* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *12-18, 20, 21, and 38-46* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *12-18, 20, 21, and 38-46* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendment and 1.132 declaration of Inventor Lawson, filed 2/24/03, has been entered.

2. Claims 12-18, 20, 21, and 38-46 are being acted upon.

3. Upon reconsideration, the previous rejection of Claims 42 and 43 under the first paragraph of 35 U.S.C. 112 for the recitation of the phrase "not sterilized" has been withdrawn.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims Claims 12-18, 20-21, 38-43, and newly added Claims 44-46, stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,026,728, (of record) in view of Caughey et al. (of record) or Gibson et al. (of record) or U.S. Patent No. 4,455,298 (of record), for the reasons set forth in Papers No. 10, 17, 22, and 26, mailed 9/26/00, 8/14/01, 3/22/02, and 10/17/02, respectively.

Applicant arguments, filed 2/24/03, have been fully considered but are not found persuasive. Applicant continues to argue that the combination of DMG and PCE comprises significant advantages which would not have been expected from the prior art. Applicant has submitted a 1.132 declaration by Inventor Lawson as additional support. Applicant argues "The data considered as a whole establish unexpected, advantageous properties representative of the full scope of the claimed subject matter and, thus, prove the nonobviousness of the claimed invention."

Applicant continues "In the Office Action, it was alleged that the advantages shown are only "modest" and cannot be considered unexpected. Applicants respectfully disagree. The data show significant activity for treating lupus conditions in the prevalent animal model used for modeling treatment of lupus in humans, as established in Dr. Lawson's newly submitted declaration (see pages 1-2 and the beginning of the Discussion section)." Applicant continues discussing the results set forth in the declaration.

A review of Inventor Lawson's declaration reveals that the assertedly unexpected results set forth in said declaration cannot be attributed to the claimed invention "at the time the invention was made" as would be required to establish nonobviousness. That is, post-filing data gathered under conditions not set forth in the specification cannot establish that the claimed invention was nonobvious at the time of the invention. Note that Example 2 of the specification sets forth the results of a single experiment in which MRI-lpr (presumably MRL/lpr) mice were "given a PCE-mouse chow mix and DMG water." There is no disclosure of the amount of PCE in the feed. It is disclosed that the DMG water was "mixed with 34 mg/L of DMG." From this disclosure it can be concluded that the absolute maximum DMG concentration in the water could only have been 0.33mM, (M.W. DMG = 103 g/mol) before dilution (the stock solution was mixed in water). The disclosure then indicates that it was estimated that the subject animals "consumed about 1-3 mg/day of DMG and 2-6 mg/day of PCE." These parameters are compared to those taught in the instant declaration of Inventor Lawson, "In our studies, discussed in more detail below, significantly lower levels of anti-nuclear antibodies were determined in animals receiving orally more than 100mM dimethyglycinc (DMG) measured in their drinking water in addition to a Perna-mouse chow mixture which contained about 40% Perna powder compared to control MRL lpr/lpr mice." The declaration goes on to teach that the actual Perna-mouse chow mixture in most experiments was 41% Perna. Additionally, the declaration discuses results of experiments that are not considered in the specification. For example, disclosures regarding skin lesions, spleen weight, and kidney pathology are all absent in the specification. Clearly then, because different parameters were used and different data was collected, the experiments of the declaration are not the experiments of the specification, and the results of the experiments discussed in the declaration cannot be said to have been known at the time of the invention. Thus, they cannot be used to support an argument of the nonobviousness of the claimed invention at the time of the invention.

Applicant argues "It was further alleged that the claims are not commensurate in scope with the unexpected results shown and that the particular experimental model, product composition and method of administration by which the unexpected results were obtained must be considered ... The law requires only that the unexpected results be significant and reasonably representative of the scope of the claimed subject matter; see, e.g., In re Kollman, 201 USPQ 193 (CCPA 1979)." Applicant further argues "The showings here are reasonably representative of the entire claimed scope at least because: 1) MRL/lpr mice are the accepted model in the art for human lupus conditions, 2) the prior art gives no hint of anti-lupus activity for Perna, thus any such activity demonstrated by the combination of DMG and Perna could not have been expected, and 3) the combined data of the specification and Dr. Lawson's declaration shows such advantages in a significant number of tests.

Regarding 1), while the MRL/lpr model may be accepted as a lupus model, it is noted that the experiments in the specification were ended before the disease could develop. As set forth in Inventor Lawson's declaration, the lupus syndrome begins in MRL mice after 12 weeks of age. It is curious then that the experiments disclosed in the specification were ended just at 12 weeks. It would seem most logical to simply administer the claimed composition and document that treated mice appeared healthier, i.e., developed less severe disease than controls. Instead, the disclosed experiments were ended before the onset of disease and parameters such as serum cytokine and antibody concentrations were measured that were then disclosed as "indicative of a shift from a Th2 response to a Th1 response" which then supposedly relates to treatment of the disease.

Regarding 2), Perna is well-known as an anti-inflammatory agent and it is equally well-known that SLE is often treated with anti-inflammatory agents, thus the obvious nature of the claimed composition.

Regarding 3), the value of Inventor Lawson's declaration in establishing support for an argument of the nonobviousness of the claimed invention has been discussed above. The experiments of the declaration are not commensurate in scope with those of the specification.

Further regarding Applicant's assertion that "The data considered as a whole establish unexpected, advantageous properties representative of the full scope of the claimed subject matter and, thus, prove the nonobviousness of the claimed

invention", as set forth above, the experiments of the specification are performed at single, unknown concentrations of Perna and DMG. The claims however, encompass *all* concentrations of both Perna and DMG. It is noted that dependent Claim 44 "limits" the claimed concentrations to a 500-fold range. Clearly then, the independent claims are intended to encompass much more than this. Accordingly, it remains the Examiner's position that Applicant has not established "advantageous properties representative of the full scope of the claimed subject matter".

Applicant argues "That the references may suggest that both Perna and DMG are anti-inflammatories does not end the inquiry, as implied in the Final Office Action ... if applicants can show that their combination provides other properties that would not have been expected by one of ordinary skill in the art, they are deserving of patent protection."

It is the Examiner's position that the last assertion is simply untrue. Evidence of unexpected results is but one factor in weighing nonobviousness. Said factor alone does not require that the Applicant be granted a patent, see MPEP 716.02(c) "Where the unexpected properties of a claimed invention are not shown to have a significance equal to or greater than the expected properties, the evidence of unexpected properties may not be sufficient to rebut the evidence of obviousness. *In re Nolan*, 553 F.2d 1261, 1267, 193 USPQ 641, 645 (CCPA 1977)."

Applicant argues "The Office Action continues to dismiss the evidence from the Belkowski disclosure, which actually teaches away from the claimed invention."

It remains the Examiner's position that the inconclusive results achieved by Belkowski in the unrelated collagen-induced arthritis model cannot be said to teach away from the claimed composition but instead, said results should be considered neutral, i.e., they neither teach, nor teach away from, the claimed invention.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 12-18, 20-21, 38-43, and newly added Claims 44-46, are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, in Claims 12 and 15, the phrase "suitable for enteral but not parenteral administration" for the reasons set forth in Paper No. 26, mailed 10/17/02.

Applicant arguments, filed 2/24/03, have been fully considered but are not found persuasive. Applicant argues "The recitations of "enteral but not parenteral administration" forms and "not sterilized" forms in the claims are not new matter. Applicants clearly stated in their last response that the recitations were supported by the disclosure, albeit not literally. If they are supported by the disclosure, it follows that they are not new matter."

It is the Examiner's position that Applicant's assertion, no matter how "clearly stated", that a recitation is not new matter does not automatically render it so.

Applicant argues "When a disclosure recites an element as being optional, it adequately describes under 35 U.S.C. § 112, first paragraph, both the option of inventions meeting the recitation of that element and the option of inventions not meeting the recitation of that element; see, e.g., Ex parte Cordova, 10 USPO 2d 1949 fBd. App. 1988). And Ex parte Wu, 10 USPQ 2d 2031 (Bd. App. 1988)."

Note that Applicant has used the term "both" in the instant argument, i.e., indicating two mutually exclusive options, as in sterile or not sterile. Accordingly, the rejection has been withdrawn as regards the recitation of "not sterilized". However, in the case of enteral and parenteral, the options are not so simple, nor are they mutually exclusive. Unlike the situation wherein a composition would be either sterile or not sterile, i.e, where there exist only two options, in the case of enteral versus parenteral, there actually exists three options. A composition might be suitable for only enteral administration, or a composition might be suitable for only parenteral administration, or a composition might be suitable for either

form of administration. The situation might be visualized as two overlapping circles (one representing the enteral subgenus and one representing the parenteral subgenus); Applicant is attempting to claim the portion of the enteral circle (subgenus) that does not overlap with the parenteral circle (subgenus). See for example Applicant's argument in which it states that "parenteral forms must be sterile, ... enteral forms need not be sterile." The clear implication of the argument is the fact that enteral forms *may* be sterile (thus the clear overlap of the subgenuses). Accordingly, Applicant is claiming an even more restrictive subgenus (nonparenteral enteral) that is not disclosed in the specification.

Additionally, Applicant "strongly protests" the previous discounting of the previously submitted declaration of Inventor Kendall, wherein the Inventor asserted that the recitation of "enteral but not parenteral" is adequately described in the specification.

Applicant is advised that the declaration was not "discounted", but rather it was fully considered and found unconvincing and inadequate (for the reasons of record) for the withdrawal of the rejection. Applicant's concerns regarding an apparent assumption that the Examiner concluded that the Inventor made willful false statements are unfounded.

Applicant argues "how one of ordinary skill in the art would have considered the disclosure is the issue at hand and the issue addressed by the declaration, thus, he [Inventor Kendall] is established as an "expert" for this purpose."

Applicant is advised that Inventor Kendall's declaration says what it says, "The following statements are not made as an expert in the field of the invention claimed in the above-identification application." The logic of Applicant's argument seems to be that because the Inventor is only one of ordinary skill in the art (and not an expert) then he would better know what one of ordinary skill in the art would know. Said argument is not found to be convincing.

Finally, Applicant argues that Inventor Lawson confirms Inventor Kendall's opinion.

It is the Examiner's position that one Inventor's opinion of the other Inventor's non-expert opinion does not strengthen their combined opinion such that the rejection must be withdrawn.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday and alternate Fridays from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Technology Center 1600 at 703-872-9306 (before final) and 703-872-9307 (after final).

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600
June 8, 2003